Three new α-glucosidase inhibitors from guggul, the oleogum resin of *Commiphora wightii*

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Abstract

Three new compounds; *epi*-mukulin, (*Z*)- $\Delta^{1,2}$ dehydroguggulsterone and $\Delta^{6,7}$dehydro-20-hydroxygugglsterone were isolated from the *n*-hexane-soluble fraction (HSF) of the methanol extract of guggul, the oleogum resin of *Commiphora wightii* together with six known compounds; diasesartemin, (+)-*epi*-magnolin, (+)-diayangambin, gugglsterol I, (*E)*-guggulsterone and *(Z)*- guggulsterone. Their structures were elucidated on the basis of different spectroscopic data. α-Glucosidase inhibitory effects of HSF and the isolated compounds were evaluated calorimetrically. The HSF showed significant a-glucosidase inhibitory effect [IC_{50} value of 140 μg/ml ($p< 0.05$)]. Under the assay conditions, diasesartemin (IC_{50} = 60.6 ± 0.01 µM) was found to be more potent than the positive control, acarbose (IC_{50} = 92.94 ± 0.01 µM); a known α-glucosidase inhibitor ($p<0.05$). The IC_{50} values of *epi*-mukulin and (*Z*)-guggulsterone were found to be 159.33 and 132.14 µM, respectively. Other compounds showed weak α-glucosidase inhibitory effects; < 30% inhibition of the enzyme activity at 0.1 mg/ml.

Keywords: guggul, *Commiphora wightii,* lignan, sterol, a-glucosidase.

1. Introduction

Guggul; the oleogum resin of *Commiphora wightii* (Arnott.) Bhanol. (Burseraceae) is produced by drying the milky-white sap of the tree (15-20 years old) for one year (Masten, 2005 and Hanuš *et al*. 2005). In Ayurvedic medicine, guggul has been traditionally used for mitigating metabolic disorders; obesity, inflammation, hypercholesterolemia and atherosclerosis. Number of ketosterols and lignans isolated from guggul were found to be responsible for demonstrating such beneficial effects (Arora *et al.* 1971 and 1972, Kimura *et al.* 2001 Francis *et al*. 2004). Postprandial hyperglycemia (PPHG) is one of the metabolic abnormalities that may lead to the development of cardiovascular complications in diabetic patients (Mooradian and Thurman, 1999). PPHG cannot be controlled by commonly used anti-diabetic drugs such as biguanides, sulfonylureas, or thiazolidinediones. However, α-glucosidase inhibitors (αGIs) like acarbose, are known to specifically reduce PPHG primarily by interfering with the carbohydrate digesting enzymes and delaying glucose absorption (Godbout and Chiasson, 2001). Acarbose has also been shown to decrease the risk of progressing to diabetes in subjects with impaired glucose tolerance (IGT) (Nishioka *et al*. 1997 and 1998).

In the course of our study on traditionally used medicines (Kawahata *et al.* 1996, Meselhy *et al.* 2005 and El-Mekkawy *et al.* 2009) we report here the isolation of four lignans and five sterols from the hexane-soluble fraction of the methanol extract of guggul and their α-glucosidase inhibitory activities.

2. Results and discussion

2.1. Identification of the isolated compounds

The *n*-hexane-soluble fraction of the methanol extract of guggul; the oleogum resin of *C. wightii*; was subjected to column chromatography over normal phase and reversed-phase Silica gel, followed by HPLC to afford three new compounds (**1**, **5** and **6**) and six known ones (**2**, **3**, **4, 7, 8** and **9**). The spectral data of the known compounds were found identical with those reported for diasesartemin (**2**), (+)-*epi*-magnolin (**3**), (+)-diayangambin (**4**) and gugglsterol I (**7**), (*E*)-guggulsterone (**8**) and (*Z*)- guggulsterone (**9**) by direct comparison of their spectral data with literature values (Patil *et al*., 1972; Bajaj and Dev, 1982; Benn and Dodson, 1964; Kimura *et al*., 2001). The structure determination of the three new compounds is prescribed as follows.

Compound **1** showed a molecular ion peak at *m/z* 484 $[M]^+$ in the EIMS corresponding to the molecular formula $C_{27}H_{32}O_8$, which was further confirmed by HR-EIMS. NMR spectral data of **1** showed signals typical for *epi*-type lignan (Ayres and Loike, 1990) with chemical shift values similar to that of **3** (Miyazawa *et al.* 1994 and Estrada-Reyesa *et al.* 2002) and to less extent to those of **2** and **4** (see experimental). Namely, signals for two methines at δ_H 2.90 (dd, *J*= 14, 7) for H-1 (C-1 at δ_C 50.1) and δ_H 3.32 for H-5 (C-5 at δ_C 54.5), two oxymethins at δ_H 4.40 for H-2 (C-2 at δ_C 87.9) and 4.80 for H-6 (C-6 at δ_C 82.0), two oxymethylens at δ_H 3.34 and 3.86 for H_2-4 (C-4 at δ_C 71.0, t) and; 3.92 and 4.18 for H_2-8 (C-8 at δ_C 69.7, t), and signals for two 1,3,4,5- and 1,2,4,5- tetrasubstituted phenyl groups [δ_H 6.57 (2H, H-2″ and 6″), δ_H 6.52 and 6.59 (H-3′ and H-6′, respectively)]. In addition, the ^{1}H-NMR spectrum of **1** analyzed by ^{1}H-^{1}H COSY and HMQC showed signals ascribed for an isoprenyl moiety [δ_H 1.67, 1.74 (3H each), 4.47 (2H, d, *J*= 8 Hz) and 5.58 (1H, t, *J*= 7 Hz)], three methoxyl groups [singlets at δ_H 3.86 (6H) and 3.92 (3H)], and a dioxomethylene group [δ_H 5.97 (2H, s), δ_C 101.8 (t)]. Long range correlations observed in the HMBC spectrum of **1** confirmed the substitution of ring A with three methoxyls, and substitution of ring B with an isoprenyl moiety at C-2' [correlation between ^{1}H signal at δ_H 4.47 (H-1''') and ^{13}C signals at 138.0 (C- 3''') and 148.8 (C-2')] and a dioxomethylene group. The optical rotation of **1** was found to be (+ 46.6^o). From these findings and by comparison to the spectral data of **3**, the structure of compound **1** was confirmed and determined as shown in Fig. 1, and was given the name *epi*-mukulin (**1**).

Compound **5** showed a molecular ion peak at *m/z* 310.19012 $[M]^+$ in HR-EIMS consistent with the molecular formula $C_{21}H_{26}O_2$ (Calcd 310.19328). Most of the NMR spectra of **5** were found to be similar to that of (*E*)-gugglsterone (**8**) and (*Z*)-gugglsterone (**9**) (Meselhy, 2003) except for the appearance of ^{1}H signals at δ_H 7.05 (1H, d) and 6.25 (1H, dd), and the corresponding ^{13}C signals at δ_C 155.1 (d) and 130.8 (d) assigned to an additional double bond in ring A in the structure of **5** ($[M]^+$ of **5** is 2 mass units less than that of (*E*)-gugglsterone and (*Z*)-gugglsterone). The geometry of C-17(20) double bond in **5** was established by carrying out the NOE difference experiment. Irradiation of the proton signal at δ_H 5.70 (H-20) led to significant enhancement of the ^{1}H signal at δ_H 1.40 (H_a-12) and 0.99 (H_3-18), while irradiation of H_3-21 (δ_H at 2.07) enhanced the C-20 proton signal. Accordingly, geometry of C-

17(20) double bond was established to be *Z*, similar to that in (*Z*)- gugglsterone (**9**), and the structure of **5** was established to be pregna-1,4-diene-3,16-dione and given the name (*Z*) $\Delta^{1,2}$-dehydrogugglsterone.

The NMR spectral data of compound **6** suggested a 21-ketosteroid skeleton with α,β-unsaturated ketone in ring A [signals for an α,β-unsaturated ketone (δ_H 5.75/ δ_C 123.9, 171.0, 199.2)]. Signals for three methyl groups were detected at δ_H 1.18/δ_C 17.4, δ_H 1.23/δ_C 22.8 and δ_H 2.12/δ_C 24.4. The HR-EIMS spectrum of **6** showed a molecular ion peak at *m/z* 314.22257 $[M]^+$ consistent with the molecular formula $C_{21}H_{30}O_2$ (Calcd 314.22246) and indicating 7 degrees of unsaturation. The presence of ^{13}C signals at δ_C 124.1 (d) and 130.6 (d), and the HMBC correlation between H-6 (δ_H 5.76) and carbon signals at δ_C 130.6 (d), 123.9 (s) and 171.0 (d) confirmed the presence of an additional double bond between C-6 and C-7 in Ring B. HMBC long range correlation between H_3-21 and ^{13}C signals at δ_C 49.0 (C-17) and at δ_C 63.5 (C-20), and correlation between H_3-18 (δ_H 1.18) and C-17 (δ_C 49.0) place a hydroxyl group at C-20 (δ_C 63.5). From the forgoing findings, the structure of **6** was concluded as 20-hydroxy-pregna-4,6-diene-3-one and was given the name $\Delta^{6,7}$-dehydro-20-hydroxygugglsterone.

2.2. α-Glucosidase inhibitory activity

The α-glucosidase activity was determined by measuring the release of *p*-nitrophenol from *p*-nitrophenyl-α-D-glucopyranoside (*p*-NPG, the substrate) colorimetrically at 412 nm in a microplate reader. The 50% inhibition of α-glucosidase enzyme activities (IC_{50}) of the tested samples was determined. The *n*-hexane soluble fraction of the methanol extract of guggul showed significant α-glucosidase inhibitory activity [IC_{50} = 140 µg/ml ($p < 0.05$)]. Diasesartemin (**2**) (IC_{50} = 60.6 ± 0.01 μM) was found to be more potent than the positive control, acarbose (IC_{50} = 92.94 μM); a known α-glucosidase inhibitor ($p<0.05$). The IC_{50} values of *epi*-mukulin (**1**) and (*Z*)-guggulsterone (**9**) were 159.33 and 132.14 μM, respectively. Compounds **3-8** showed very weak inhibitory effects; 20.2 - 26.9 % at a concentration of 0.1mg/ml [table 1].

3. Experimental

3.1. General

Optical rotations were measured using a JASCO DIP-360 automatic polarimeter, Tokyo, Japan. IR spectra were taken out on a JASCO FT/IR-230 IR spectrometer Tokyo, Japan. Mass spectra were measured on JEOL JMS-700 Mstation (JEOL JMS-

AX505HA, Tokyo, Japan), matrix: thioglycerol-glycerol (1:1 by vol.), acceleration voltage: 8 KV, emitter current: 3 mA, gun High Voltage: 6 KV, gas: Xe, samples were dissolved in MeOH. NMR spectra were measured on Varian Unity-400 machine, California, USA. HPLC specification: pump, Shimadzu LC-6A liquid chromatograph; UV Detector, Shimadzu SPD-6A spectrophotometric detector; column, Senshu pack pegasil ODS (20 X 250 mm); UV detection, 254 nm and the flow rate was 4 ml/min, isocratic elution system with acetonitrile/water mixture (7:3). TLC: silica gel 60 F_{254} plates (Merck) using *n*- hexane-EtOAc 1:1 (system A) and $CHCl_3$ - EtOAc 1: 2 (system B) and the spots were detected under a UV lamp and after spraying with 10 % H_2SO_4 followed by heating.

3.2. Plant materials

The oleogum resin of *Commiphora wightii* (Arnott.) Bhanol. [syn. = *C. mukul* (Hook, ex Stocks) Engl.] was purchased from Khari Baovli, crude drug market, Delhi-6, India during October 2008. The material was in the form of light to dark brown conglomerates of tears and was only slightly sticky and had a faint balsamic odor. The material was kindly identified by Prof. Javed Ahmad, Dept. of Botany, Hamdad University, New-Delhi 110062, India. A voucher specimen (number 2011006) was deposited at the Department of Pharmacognosy, Faculty of Pharmacy, Cairo University, Cairo, Egypt

3.3. Extraction and isolation

The oleogum resin (250 g) was triturated with MeOH (1 l X 4) and the combined MeOH extracts were evaporated *in vacuo* to give 56 g of a yellowish brown gum. The MeOH extract was suspended in 90% MeOH (200 ml) and partitioned with *n*-hexane (500 ml x 4). HSF was evaporated to give 15 g of a thick yellow oily residue. This residue was loaded on a Si gel column (300 g, 10 X 40 cm). Elution was carried out with *n*-hexane, *n*-hexane-EtOAc (25→60%), $CHCl_3$, 50% EtOAc in $CHCl_3$ and 50 % MeOH in $CHCl_3$ to give 22 main fractions.

Fraction Fr. 4-1 [1.0 g, eluted with *n*-hexane-EtOAc (2:1)] was further chromatographed on a Si gel column (30 g, 2.5 x 30 cm). Elution with *n*-hexane and then *n*-hexane–EtOAc (95 %→ 60%) gave 15 fractions. Subfraction Fr. 4-1-8 (180 mg), was purified by pre-HPLC (Senshu pack pegasil ODS, 50 mg/ml, injection volume 300 μl) using 70% CH_3CN in H_2O to give compounds **1** (8.5 mg), **6** (5.5 mg) and **7** (5.5 mg). Fraction 4-4 (3.0 g), eluted with *n*-hexane-EtOAc (1:1) was further

chromatographed on a Si gel column (90 g, 3.5 x 50 cm) and eluted with *n*-hexane, *n*-hexane –EtOAc (95 %→ 60%) to give 15 fractions. Preparative TLC of subfractions Fr. 4-4-3, Fr. 4-4-4 and Fr. 4-4-5 (Si gel, sys. A) afforded diasesartemin (**2**, 11 mg), *epi*-magnolin (**3**, 37 mg) and (+)- diayangambin (**4,** 30 mg), respectively.

Fraction 5 (80 mg) (50 mg/ml, injection volume 300 μl) was purified by chromatography on pre-HPLC using 65% CH_3CN in H_2O to give **5** (4 mg) and additional amounts of **4** (9 mg), **6** (19 mg) and **7** (8 mg).

***epi*-Mukulin (1)**: Amorphous white powder, $[\alpha]_D$ + 46.6° (MeOH, *C*= 0.4). UV λ_{max} MeOH nm (log ε): 225 (3.8), 252 (3.8), 270 (4.0), 300 (3.9), 365 (3.7). IR ν_{max} cm^{-1}: 3100, 1630, 1595, 1560, 1486, 1234, 1150, 885. HR-EIMS: *m/z* found 484. 21364 ($C_{27}H_{37}O_8$ requires 484.21376). ^{1}H-NMR (400 MHz, CD_3OD) : δ 1.67 (3H, s, C$\underline{H_3}$-4′′), 1.74 (3H, s, C$\underline{H_3}$-5′′); 2.92 (1H, dd, *J* = 14.0, 7.0 Hz, H-1); 3.32 (1H, m, H-5); 3.34 (1H, m, H_b-4); 3.86 (6H, s, 2 X OC$\underline{H_3}$); 3.86 (1H, m, H_a -4); 3.92 (3H, s, OC$\underline{H_3}$); 3.92 (1H, m, H_b -8); 4.18 (2H, br d, *J*= 10.0 Hz, H_a-8); 4.40 (1H, d, *J*= 7.0 Hz, H-2); 4.47 (2H, d, *J*= 8.0 Hz, H-1′′); 4.8 (1H, d, *J* = 6.0 Hz, H-6); 5.58 (1H, t, *J*= 7.0 Hz, H-2′′); 5.97 (2H, s, H-8′); 6.52 (1H, brs, H-3′); 6.57 (2H, s, H-6′′ , H-2′′); 6.59 (1H, brs, H-6′). ^{13}C-NMR (125 MHz, CD_3OD): δ 17.9 (q, C-4'''); 25.8 (q, C-5'''); 50.1 (d, C-1); 54.5 (d, C-5); 56.1 (q, 4''- O$\underline{C}H_3$, 5''- O$\underline{C}H_3$); 56.6 (q, 3''- O$\underline{C}H_3$); 69.7 (t, C-8); 71.0 (t, C-4); 82.0 (d, C-6); 87.9 (d, C-2); 91.6 (t, C-1'''); 99.8 (s, C-3'); 101.8 (t, C-8'); 102.9 (d, C-2'', C-6''); 104.9 (s, C-6'); 120.7 (d, C-2'''); 132.9 (s, C-1'); 134.1 (s, C-5'); 136.4 (d, C-4''); 136.5 (d, C-1''); 138.0 (s, C-3'''); 143.5 (s, C-4'); 148.8 (s, C-2'); 153.8 (s, C-3''); 153.8 (d, C-5'').

(*Z*) $\Delta^{1,2}$ Dehydroguggulsterone (5): Amorphous pale yellow powder, $[\alpha]_D$ + 30.5° (MeOH, *C*= 0.55). UV λ_{max} MeOH nm (log ε): 220 (3.8), 250 (4.0), 260 (4.2); IR ν_{max} cm^{-1}: 1670, 1630, 1590, 1450, 1375, 1225, 1077. HR-EIMS: *m/z* found 310.19012 ($C_{21}H_{26}O_2$ requires 310.19328). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.99 (3H, s, C$\underline{H_3}$-18); 1.03 (1H, m, H-9); 1.20 (1H, m, H_a-7); 1.26 (1H, m, H-14); 1.28 (3H, s, C$\underline{H_3}$-19); 1.40 (1H, m, H_a-12); 1.65 (1H, m, H-8); 1.82 (2H, m, H-11); 1.88 (2H, m, H_b-12 & H_b-7); 2.07 (3H, d, *J*= 8.0 Hz, C$\underline{H_3}$-21); 2.21 (1H, m, H_a-6); 2.40 (1H, m, H_b-6); 2.47 (1H, dd, *J* = 12.0, 3.6 Hz, H_a-15); 2.51 (1H, dd, *J* = 12.0, 13.6 Hz, H_b-15); 5.70 (1H, q, *J* = 7.5 Hz, H-20); 6.09 (1H, brs, H-4); 6.25 (1H, dd, *J*=10.0, 2.0 Hz, H-2); 7.05 (1H, d, *J*= 10.0 Hz, H-1). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 14.1 (q, C-21); 18.7 (q, C-18); 19.6 (q, C-19); 22.5 (t, C-11); 32.6 (t, C-7); 33.3 (t, C-6); 34.5 (d, C-8); 35.3 (t,

C-15); 39.3 (t, C-12); 43.3 (s, C-13); 43.5 (s, C-10); 48.6 (d, C-14); 52.1 (d, C-9); 124.2 (d, C-4); 127.8 (d, C-20); 130.8 (d, C-2); 147.5 (s, C-17); 155.1 (d, C-1); 168.3 (s, C-5); 186.2 (s, C-3); 207.4 (s, C-16).

$\Delta^{6,7}$ **Dehydro-20-hydroxygugglsterone (6)**: Amorphous pale yellow powder, $[\alpha]_D$ + 27.6° (MeOH, *C*=0.75). UV λ_{max} (MeOH) nm (log ε): 210 (3.7), 245 (3. 8), 270 (4.0); IR ν_{max} cm^{-1}: 3270, 1650, 1560, 1450, 1375, 1225, 1077. HR-EIMS: *m/z* found 314.22257 ($C_{21}H_{30}O_2$ requires 314.22246): ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.01 (1H, m, H-9); 1.07 (1H, m, H_a-16); 1.18 (3H, s, C$\underline{H_3}$-18); 1.23 (3H, s, C$\underline{H_3}$-19); 1.26 (1H, m, H_b-16); 1.30 (1H, m, H-14); 1.40 (1H, m, H_b-11); 1.46 (2H, m, H_a-15& H_b-12); 1.65 (1H, m, H_a-11); 1.7 (1H, m, H_b-1); 1.88 (2H, m, H_b-15 & H_a-12); 2.02 (1H, m, H_a-1); 2.08 (1H, m, H-8); 2.12 (3H, s, C$\underline{H_3}$-21); 2.40 (1H, dd, *J* = 12.0, 3.6 Hz, H_b-2); 2.53 (1H, dd, *J* = 12.0, 13.6 Hz, H_a-2); 5.18 (1H, brs, H-20); 5.72 (1H, d, *J* = 10.0 Hz, H-7); 5.75 (1H, s, H-4); 5.76 (1H, d, *J* = 10 Hz, H-6). ^{13}C-NMR (125 MHz, $CDCl_3$): δ_C 17.4 (q, C-18); 22.8 (q, C-19); 24.4 (q, C-21); 25.0 (t, C-1); 31.9 (t, C-11); 32.8 (t, C-2); 33.9 (d, C-8); 35.5 (t, C-12); 38.1 (s, C-13); 38.6 (t, C-16); 39.3 (t, C-15); 43.9 (s, C-10); 49.0 (d, C-17); 53.6 (d, C-9); 56.0 (d, C-14); 63.5 (d, C-20); 123.9 (d, C-4); 124.1 (d, C-6); 130.6 (d, C-7); 171.0 (s, C-5); 199.5 (s, C-3)

3.4. Enzyme and substrate

α-Glucosidase enzyme (EC 3.2.1.20) and the substrate; *p*-nitrophenyl *α*-D-glucopyranoside (*p*-NPG), were purchased from Sigma Chemical Co., (St Louis, MO 63103, USA). The positive control, acarbose was purchased from Bayer Pharmaceuticals Pty, Ltd (USA).

3.5. Assay for α-glucosidase inhibitory activity

The assay method was adopted from Collins *et al.* (1997) and modified accordingly to suite microtiter reading. The glycohydrolase assay was performed in 96-well microtiter plates. The enzyme was diluted in 50 mM Mes-NaOH, pH 6.5. The extracts were allowed to interact with the enzyme at room temperature for 5 minutes before the reaction was started by the addition of the substrate (*p*-NPG). The total reaction volume was 0.2 ml. The reaction was allowed to proceed at room temperature for 15 minutes before it was stopped by the addition of 60 μl 2M glycine-NaOH, pH 10. The assay was performed in triplicates. The final concentration of tested samples in the wells ranged from 0.02 to 200 μg/ml. Acarbose (positive control) and the tested compounds were used in concentrations range from 0.01 to 100

μM. The yellow coloured product (*p*-nitrophenol) was measured in a Bio-Tek® model microplate reader at 412 nm (reference 490 nm). Results were analysed using the formula:

% Inhibition = [Sample absorbance/ Control absorbance] X 100

The fifty percent inhibitory concentration (IC_{50}) of the active compounds against yeast glucosidase was calculated.

3.6. Statistical analysis:

The results were expressed as the mean ± standard deviation (S.D.). The means were compared using ANOVA test (MSTATC software, East Lansing, MI, USA) and the Duncan's Multiple range test. Values were determined to be significant when *p* was less than 0.05 ($p<0.05$).

4. Conclusion

Diabetes is known as a multifactorial disease and its treatment is complicated by several factors inherent to the disease, and the elevated postprandial hyperglycemia (PPHG) is one of the risk factors. PPHG is elevated by the action of glucosidases, a class of enzymes that help in the breakdown of starch into simple sugars such as maltose and glucose that can be absorbed into the bloodstream (Bhat *et al.*, 2008). Glucosidase inhibitors such as acarbose (Glucobay), voglibose (Basen) and miglitol (Glyset) are on the market as the therapeutic agents of diabetes (Kuriyama *et al.*, 2008). These known drugs however, are known to be associated with gastrointestinal side effects such as abdominal pain, flatulence, diarrhea in the patients (Bhat *et al.*, 2008). In this context, Nishioka *et al.* (1997) and Yoshikawa *et al.* (1998) isolated flavonoids, N-*p*-coumaroyl tyramine and kotalanol from plants which have been reported to be strong inhibitors of α-glucosidase.

The present study demonstrated the α-glucosidase inhibitory activity of the *n*- hexane-soluble fraction of the methanol extract of guggul and the compounds isolated thereof, where *epi*-mukulin (**1**), diasesartemin (**2**) and (*Z*)-guggulsterone (**9**), showed promising inhibitory effects. Accordingly, further study will be carried out in order to develop lead compounds based on their chemical structures.

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Captions:

Table 1 : Inhibitory Effects of the HSF of the methanol extract of guggul; the oleogum resin of *C. wightii* and its isolated compounds on α-glucosidase enzyme

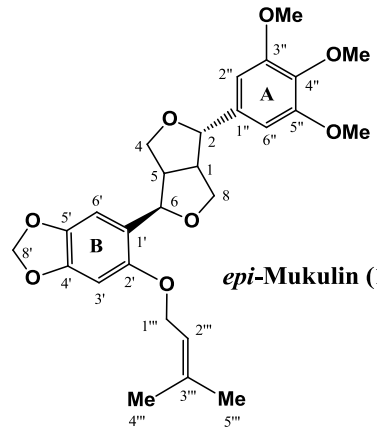
Figure 1 : Chemical structures of the isolated compounds from guggul; the oleogum resin of *C. wightii*

Table 1 Inhibitory Effects of the HSF of the methanol extract of guggul; the oleogum resin of *C. wightii* and its isolated compounds on α-glucosidase enzyme

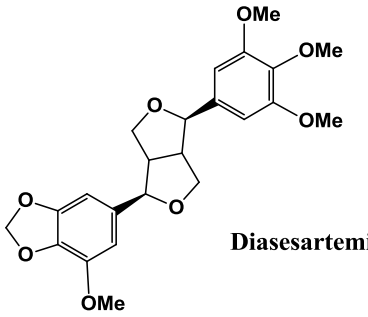
Tested Samples	% inhibition (0.1 mg/ml)	IC_{50} (µM ± S.D.)
Extract	75.35 *	140.10 ± 0.08 [a]
Comp. **1**	80.55	159.33 ± 0.04
Comp. **2**	90.43	60.55 ± 0.01
Comp. **3**	20.21	ND
Comp. **4**	22.60	ND
Comp. **5**	25.55	ND
Comp. **6**	26.89	ND
Comp. **7**	21.18	ND
Comp. **8**	16.68	ND
Comp. **9**	85.90	132.14 ± 0.19
Acarbose (positive control)	80.95	92.94 ± 0.01

Values are the mean of triplicate measurements± S.D.

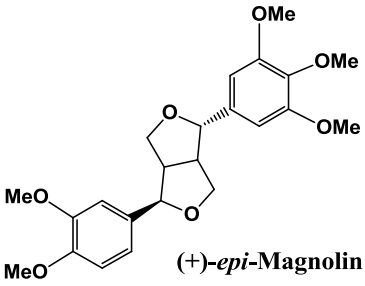
* Extract's concentration is 0.2 mg/ml, [a]µg/ml; ND: not determined.



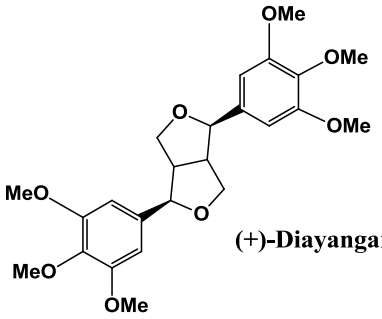
epi-Mukulin (1)



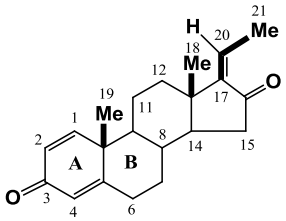
Diasesartemin (2)



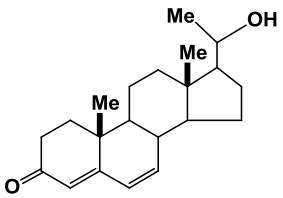
(+)-*epi*-Magnolin (3)



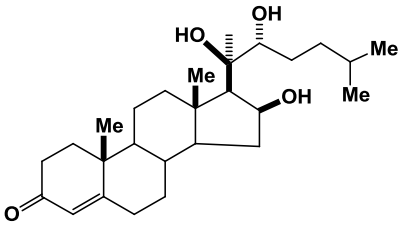
(+)-Diayangambin (4)



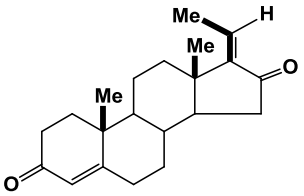
(*Z*) $\triangle^{1,2}$ Dehydroguggulsterone (5)



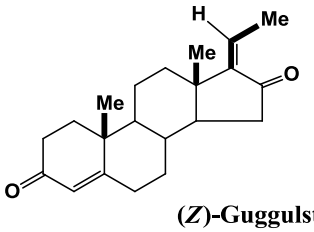
$\triangle^{6,7}$ Dehydro-20-hydroxygugglsterone (6)



Guggulsterol-I (7)



(*E*)-Guggulsterone (8)



(*Z*)-Guggulsterone (9)

Figure 1 Chemical structures of the isolated compounds from guggul; the oleogum resin of *C. wightii*